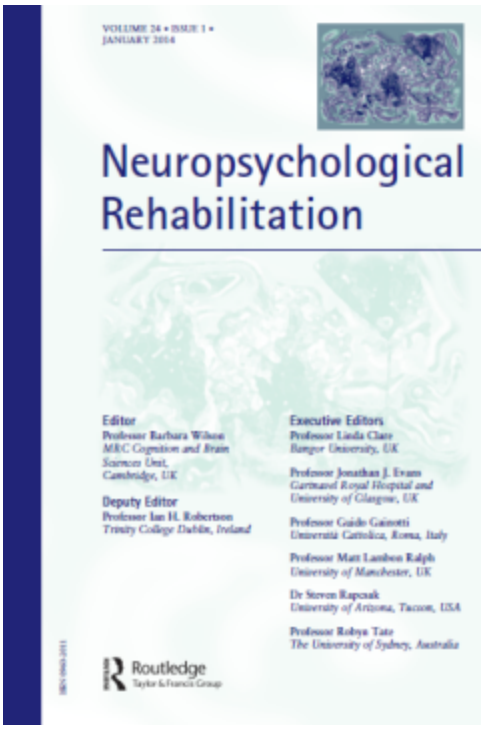

Neuropsychological consequences of Covid-19

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Editorial for Neuropsychological Rehabilitation

Neuropsychological consequences of Covid-19

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There are seven coronaviruses of which four are relatively mild. The three acute ones are: SARS (Severe Acute Respiratory Syndrome); MERS (Middle East Respiratory Syndrome; and the one causing the current pandemic, SARS-Covid-2, which is the technical name for the new virus. The illness caused by SARS-Covid-2 is Covid-19.

Many Covid-19 survivors who have been seriously ill are likely to need ongoing help. We know that several body systems can be affected by Covid-19, including the respiratory, circulatory, and digestive systems. Central nervous system involvement has also been documented. In some cases the virus can directly affect the brain, with both infection and inflammation-based mechanisms possible, and a range of secondary neurological effects as part of broader systemic illness have also been reported. As a result, alongside well-acknowledged difficulties with fatigue and deconditioning, people recovering from Covid-19 may have cognitive, emotional and behavioural problems that require a referral to neuropsychology and/or neuropsychiatry services. We do not yet know how many people are affected nor how long their problems will last, but a number of reviews based on the early studies of people with Covid-19, as well as related conditions, have provided some initial pointers.

Within the UK, cases of those with Covid-19 admitted to hospital and presenting with neurological and neuropsychiatric features have been carefully profiled as part of the Coronerve national registry study. Varatharaj et al. (2020) reported that of 153 cases submitted to the Coronerve registry, 125 had complete data. Of these 125, they identified that 62% had suffered a cerebrovascular event and of these, 74% were ischemic, 12% haemorrhagic, 1% had vasculitis and the remainder other cerebrovascular events. Of the 125, 31% presented with altered mental status, and of this subgroup, encephalitis was identified in 18%, unspecified encephalopathy in 23% and neuropsychiatric disorder in 59%. Of the 23 cases classified as neuropsychiatric, 43% were described as having psychosis, 26% neurocognitive disorder, and 30% other psychiatric disorders. Finally, 5% of the total were classified as having a peripheral disorder and 2% other neurological disorder.]

Considering the international as well as UK data, Ellul et al (2020a) examined case reports and series totalling 901 patients with neurological manifestations of Covid-19 up to May 2020, They report that cerebrovascular events have been unexpectedly common, being reported in 96 patients. They also highlighted that encephalopathy is relatively common, being reported for 93 patients in total. This figure includes 16 (7.5%) of 214 hospitalised COVID-19 patients in Wuhan, China, and 40 (69%) of 58 in intensive care with COVID-19 in France. Encephalitis has been documented in eight patients, and Guillain-Barré syndrome in 19 patients. It is important to note that there is some doubt regarding whether or not Covid-19 was a causal factor in all of these cases and some case reports have provided insufficient detail to establish causality (see Ellul et al., 2020b for guidance). Nonetheless, it is clear that 'neuro-covid' cases exist and appropriate care and rehabilitation pathways are needed for these patients.

A recent review by Ritchie, Chan and Watermeyer (2020) is informative in considering the broader neuropsychological aspects of Covid-19. They cite a preliminary study documenting that 70% of people with Covid-19 admitted to intensive treatment units required mechanical ventilation, and link this to the

literature on cognition in acute respiratory distress syndrome (ARDS). They summarise that up to 78% of people with ARDS had cognitive problems a year post-discharge and approximately 50% at two years. Self-reported everyday memory failures, such as forgetting medication and appointments, have been found to persist in patients 5 years post-discharge. Furthermore, a proportion of those who have spent time in intensive care (a population that overlaps with ARDS) are known to experience lasting cognitive impairment. For example Wolters et al. (2013) found in a systematic review of the literature that, although estimated prevalence of cognitive impairment varied between 4-62% in patients followed up at between 2-156 months, the majority of studies have identified that critical illness and associated treatment is linked with lasting cognitive deficits. Together, these findings suggest that enduring cognitive deficits are likely to be common in people who have had severe forms of Covid-19 even without an obvious neurological presentation in the acute stages.

It is, of course, also the case that some people with pre-existing neurological conditions have become unwell with Covid-19, and there are indications that comorbidities may lead to more severe forms of the illness (e.g. Louapre et al., 2020, found this pattern in people with multiple sclerosis). Though cognitive outcomes in such groups have not, to our knowledge, been studied our clinical impression is that cognition has been vulnerable to accelerated decline in such cases at least in the early stages of recovery.

We do not yet have a good understanding of the profile of cognitive deficits resulting from Covid-19. The studies previously cited suggest problems with memory, attention and information processing, and executive function, are likely to be particularly prevalent (e.g. based on the hypothesized sensitivity of the hippocampus to the virus, and the ARDS and critical illness literature). However, it follows from the wide variety of neurological and neuropsychiatric presentations reported that the cognitive profiles are also likely to be diverse and as neuropsychologists we must be alert to the possibility that rare and/or difficult to identify syndromes may result. An Indian colleague, Jwala Narayanan, has reported a 62 year old patient who developed Covid-19, then had a stroke

and was left with Balint's Syndrome (Narayanan, Wilson & Evans, in press). As far as we are aware, this is the first case of this rare syndrome to be reported in a patient diagnosed with Covid-19.

The mental health impacts of Covid-19 can also be estimated to be high, based on knowledge accrued from the earlier pandemics, and the literature on recovering from critical illness. Ritchie et al. (2020) cite research on psychological distress in MERS and SARS, identifying that up to 70% of people with confirmed MERS showed psychiatric symptoms including psychosis and hallucinations during their admission, and that in a study of 90 people with SARS, 59% were diagnosed with a psychiatric disorder, which persisted in a third of cases 2-3 years after the illness. A report by the British Psychological Society (BPS) has also emphasized the potential for ongoing difficulties with mood, anxiety, and fatigue likely to be experienced be people recovering from less severe cases of Covid-19, for example those hospitalized but not in intensive care (BPS, 2020), and by extension these may be experienced at a lower rate but by a higher number of people who were unwell but were not hospitalised. Family members and carers may also experience anxiety, stress, and problems with mood and sleep, and these could well be exacerbated by restrictions on visiting family members in hospital.

Strokes are not uncommon (Goldberg 2020). Indeed, Covid-19 may even *present* as stroke as reported in four patients in the USA (Avula et al., in press). The Varatharaj et al. paper referred to above found that cerebrovascular events predominated in patients over 50 years of age. Altered mental status, despite being present in all ages and most frequently reported in those in their 70s, had a disproportionate representation relative to cerebrovascular events in the young.

All of the above reports and observations suggest that many survivors of Covid-19 are likely to require neuropsychological assessment and rehabilitation. At present, rehabilitation is severely underfunded. A paper from the British Society of Rehabilitation Medicine (BSRM: Phillips. Turner-Stokes, Wade and Walton

2020) stresses that rehabilitation is critical but we should expect problems when trying to offer this rehabilitation, as Covid-19 patients will provide a great challenge to the existing structures of rehabilitation. For example, many Covid-19 patients will need local, community-based rehabilitation services which are weak and often transient. If any funding is available for rehabilitation it is likely to go to those critically ill probably representing only a small minority of all patients needing rehabilitation.

The BSRM report touches on clinical psychology/neuropsychology when discussing the importance of multidisciplinary teams but it does not recognize the importance of neuropsychiatry and clinical psychology in relation to the management of the mental health needs of these patients or stress the importance of clinical *neuropsychology* when dealing with the cognitive issues, which is our main area of expertise. In particular, the organization of services around diagnoses has resulted in some Covid-19 patients who exhibit cognitive deficits being unfairly restricted from accessing community neurorehabilitation services because they do not have a formal neurological diagnosis. Furthermore the physical rehabilitation teams, which Covid-19 patients are referred to, are typically unskilled in the management of cognitive deficits. Covid-19 has challenged all health care providers, including rehabilitation, and will continue to do so for at least the next few years. It has precipitated rapid change and adaptation to different circumstances. We might, in the long term develop a much needed change in the attention paid to rehabilitation, leading to a better organisation and system of funding to allow for more efficient and effective use of resources around need rather than diagnosis. Such a change will benefit all patients and all parts of healthcare.

In the interim many patients are likely to require rehabilitation and there needs to be recognition by health care provides that Covid-19 patients need to be allowed to access services based on clinical need rather than diagnosis, as the long-term sequelae of the condition are still unknown. We need to provide long-term follow up with regard to neuropsychology, as we do not know how long the cognitive, behavioural and emotional problems will last.

In June, a report from Public Health England identified that people from Black Asian and Minority Ethnic backgrounds are up to twice as likely to die from Covid-19 as people from White British background (Public Health England, 2020), a pattern that had been increasingly apparent in news reports on those affected. Though the reasons behind this devastating health inequality are complex and remain under investigation, it is notable that the literature on neuropsychological aspects of Covid-19 has yet to address this issue, and it will be important to ensure neuropsychological procedures and services are culturally-informed and that their equity is monitored. This is particularly pressing given the contemporaneous increase in awareness of the shameful extent to which racism continues to exist and operate from individual through to societal levels worldwide, highlighted by the Black Lives Matter movement in response to the murder of George Floyd.

At St George's hospital in London, we are carrying out cognitive and psychological screening assessments on all post Covid-19 patients referred to the clinical neuropsychology and clinical health psychology department. We are conducting this audit in an attempt to characterise the neuropsychological needs of the people with Covid-19 seen within our department. We want to know the reasons they are referred, what type of cognitive, emotional and behavioural difficulties they face and what are the functional consequences of these problems. We also wish to discover if these difficulties persist or resolve over time. Through this audit we hope to be able to better understand the needs of this patient group, to inform the service we provide for them, and to share this knowledge with colleagues and commissioners.

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